Piastrine: Alterazioni qualitative o quantitative

THROMBOPOIETIN-PLATELET AXIS IN METABOLIC-ASSOCIATED STEATOTIC LIVER DISEASE

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Background and Aims. Metabolic-associated steatotic liver disease (MASLD) is characterized by systemic alterations involving the liver–platelet axis. Experimental evidence has demonstrated that platelets actively contribute to NASH development and progression to hepatocellular carcinoma, particularly through GPIbα-mediated inflammatory pathways. In parallel, the liver plays a central role in regulating platelet homeostasis by controlling both thrombopoietin (TPO) production and platelet clearance, supporting a bidirectional interaction between liver function and platelet biology. Thrombopoietin (TPO) regulates platelet production through its receptor CD110, while glycocalicin (GC), generated by ADAM17-mediated cleavage of the platelet receptor GPIbα, reflects platelet clearance. In this context, alterations in the TPO–GPIbα axis may represent a link between hepatic dysfunction and platelet-driven inflammation. However, the clinical relevance of these pathways, including the role of the TPO/GC balance in MASLD severity, remains poorly defined. This study aimed to investigate the association between MASLD severity and circulating levels of TPO, GC, and the TPO/GC ratio, as well as platelet expression of CD110, GPIbα, and ADAM17.

Methods. A total of 171 subjects were enrolled. They were stratified according to the presence of MASLD [without (NO) (n=42), mild MASLD (MILD) (n=64), and moderate–severe MASLD (MOD–SEV) (n=65)]. Plasma levels of TPO and GC were measured and used to calculate the TPO/GC ratio. Platelet surface expression of CD110 and GPIbα was assessed by flow cytometry, while total platelet expression of GPIbα and ADAM17 was evaluated by Western blot. Group differences were analyzed using appropriate statistical methods.

Results. Plasma TPO levels were significantly increased in subjects with moderate–severe MASLD compared with those without MASLD (MOD–SEV vs NO, P = 0.030), showing a progressive increase with disease severity; a trend was also observed when comparing MOD–SEV with MILD (P = 0.093). Plasma GC levels did not differ significantly among groups. Consequently, the TPO/GC ratio was higher in patients with moderate–severe MASLD, reaching borderline statistical significance versus controls (MOD–SEV vs NO, P = 0.050), suggesting a shift of the TPO–GPIbα axis toward increased TPO availability (Figure). The percentage of platelets expressing the TPO receptor (%CD110: MOD–SEV vs NO, P = 0.070; MILD vs NO, P = 0.094) and GPIbα (MOD–SEV vs NO, P = 0.095; MILD vs NO, P = 0.003) showed a trend toward higher values in MASLD subjects compared with controls. Conversely, the mean fluorescence intensity (MFI) of both receptors was reduced in moderate–-severe MASLD (MFI CD110: MOD–SEV vs MILD, P = 0.068; MFI GPIbα: MOD–SEV vs NO, P = 0.043; MOD–SEV vs MILD, P = 0.042), indicating receptor redistribution or remodeling (Figure). Platelet ADAM17 expression did not differ significantly among groups, whereas total GPIbα expression assessed by Western blot showed a trend toward increased levels in moderate–severe MASLD (MOD–SEV vs NO, P = 0.065) (Figure).

Conclusions. MASLD severity is associated with progressive dysregulation of the thrombopoietin–platelet axis, characterized by increased circulating TPO. Increased platelet expression of GPIbα may contribute to the enhanced thrombopoiesis in advanced disease, supporting sustained platelet production and survival. These changes occur in the absence of significant ADAM17-mediated shedding, indicating functional platelet adaptation rather than overt activation. Overall, the TPO/CD110–GPIbα axis emerges as a candidate biomarker of disease severity and a mechanistic contributor to MASLD progression.

